

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 16 February 2001 (16.02.01)	<b>Applicant's or agent's file reference</b> 00111WO
<b>International application No.</b> PCT/GB00/02302	<b>Priority date (day/month/year)</b> 14 June 1999 (14.06.99)
<b>International filing date (day/month/year)</b> 13 June 2000 (13.06.00)	
<b>Applicant</b> LIEBESCHUETZ, John, Walter et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 21 December 2000 (21.12.00)

☐ in a notice effecting later election filed with the International Bureau on:  
 \_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Pascal Piriou Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

HAY, Martin, A.  
Martin A. Hay & Co.  
13 Queen Victoria Street  
Macclesfield  
Cheshire SK11 6LP  
ROYAUME-UNI

Date of mailing (day/month/year) 22 February 2001 (22.02.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 00111WO	
International application No. PCT/GB00/02302	International filing date (day/month/year) 13 June 2000 (13.06.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address PROTHERICS MOLECULAR DESIGN LIMITED Beechfield House Lyme Green Business Park Macclesfield Cheshire SK11 0JL United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address
<input type="checkbox"/> the nationality	<input type="checkbox"/> the residence	
Name and Address	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary: Due to an assignment the above applicant has been removed from the record.		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Maria Victoria CORTIELLO
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 00/02302

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C07D211/26 C07D295/18 C07D333/38 C07D217/04 C07D213/82  
C07D209/08 C07D209/42 C07D231/56 C07D241/24 C07D317/68  
C07D209/30 C07D209/34 C07D235/06 C07D277/64 C07C237/22

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 11657 A (CREW ANDREW PHILIP AUSTIN ; JONES STUART DONALD (GB); MORGAN PHILLI) 11 March 1999 (1999-03-11) cited in the application claim 1; examples ---	1-27
X	WO 98 47876 A (AKZO NOBEL NV ; BOECKEL CONSTANT ADRIAAN ANTON (NL); GALEN PHILIPPU) 29 October 1998 (1998-10-29) page 5, line 24; claim 1; examples 111AI, 117Q, 117R ---	1-12, 25, 27
X	EP 0 617 032 A (URIACH & CIA SA J) 28 September 1994 (1994-09-28) page 7, line 1 - line 18; claim 11 page 2, line 10 - line 30 --- -/-	1, 12, 25, 27

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

1 February 2001

Date of mailing of the international search report

13/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

De Jong, B

# INTERNATIONAL SEARCH REPORT

International Application No

PC 00/02302

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C237/42 C07D211/34 C07D213/74 C07D277/28 C07D217/06  
 C07D401/14 C07D401/12 C07D333/68 C07D405/14 C07D413/14  
 C07D213/53 C07D487/04 C07D277/82 A61K31/395 A61K31/445

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 11658 A (JONES STUART DONALD ;MORGAN PHILLIP JOHN (GB); RIMMER ANDREW DAVID) 11 March 1999 (1999-03-11) cited in the application abstract	1,25,27
X	WO 97 19927 A (SMITHKLINE BEECHAM SPA ;GIARDINA GIUSEPPE ARNALDO MARI (IT); FARIN) 5 June 1997 (1997-06-05) claim 1; examples	1-12,25
X	US 5 346 907 A (BENNETT MICHAEL J ET AL) 13 September 1994 (1994-09-13) claim 1; examples 61,62	1-12,25
X	EP 0 564 924 A (MILES INC) 13 October 1993 (1993-10-13) example 14	1-12,25
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
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- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

1 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

De Jong, B

# INTERNATIONAL SEARCH REPORT

Int'l Patent Application No  
PC/GB 00/02302

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K31/496 A61P7/02

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 441 226 A (URIACH & CIA SA J) 14 August 1991 (1991-08-14) claim 1; example 11 -----	1-12, 25, 27

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- \*A\* document defining the general state of the art which is not considered to be of particular relevance
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

1 February 2001

Date of mailing of the international search report

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk  
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Fax (+31-70) 340-3016

Authorized officer

De Jong, B

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC 8 00/02302

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9911657 A	11-03-1999	AU 8875398 A AU 8875798 A EP 1012166 A EP 1009758 A WO 9911658 A	22-03-1999 22-03-1999 28-06-2000 21-06-2000 11-03-1999
WO 9847876 A	29-10-1998	AU 7648698 A EP 0975600 A ZA 9803176 A	13-11-1998 02-02-2000 21-10-1998
EP 0617032 A	28-09-1994	ES 2062943 A CA 2118831 A JP 7002841 A US 5420131 A	16-12-1994 24-09-1994 06-01-1995 30-05-1995
WO 9911658 A	11-03-1999	AU 8875398 A AU 8875798 A EP 1012166 A EP 1009758 A WO 9911657 A	22-03-1999 22-03-1999 28-06-2000 21-06-2000 11-03-1999
WO 9719927 A	05-06-1997	EP 0874827 A JP 2000512614 T	04-11-1998 26-09-2000
US 5346907 A	13-09-1994	EP 0336356 A EP 0442878 A JP 3503650 T WO 8910355 A CA 2062755 A EP 0480969 A GR 90100516 A, B IE 902295 A JP 4506660 T PT 94623 A WO 9100725 A	11-10-1989 28-08-1991 15-08-1991 02-11-1989 08-01-1991 22-04-1992 10-12-1991 16-01-1991 19-11-1992 20-03-1991 24-01-1991
EP 0564924 A	13-10-1993	AT 170870 T AU 3677393 A CA 2091194 A DE 69320858 D DE 69320858 T DK 564924 T ES 2119826 T JP 6041064 A US 5686424 A	15-09-1998 14-10-1993 09-10-1993 15-10-1998 04-02-1999 07-06-1999 16-10-1998 15-02-1994 11-11-1997
EP 0441226 A	14-08-1991	ES 2019029 A ES 2027874 A	16-05-1991 16-06-1992

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 00111/WO	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/02302	International filing date (day/month/year) 13/06/2000	Priority date (day/month/year) 14/06/1999
International Patent Classification (IPC) or national classification and IPC C07D211/00		
Applicant ELI LILLY AND COMPANY et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.
  - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  21/12/2000	Date of completion of this report  21.08.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer  De Jong, B  Telephone No. +31 70 340 2833  

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02302

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-244 as originally filed

**Claims, No.:**

1-27 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/02302

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

**see separate sheet**

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	21-26
	No:	Claims	1-20,27
Inventive step (IS)	Yes:	Claims	25,26
	No:	Claims	1-24,27
Industrial applicability (IA)	Yes:	Claims	1-27
	No:	Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/02302

The following documents (D) are referred to in this communication:

D1: WO9911657  
D2: WO9847876  
D3: EP-A-617032  
D4: WO9719927  
D5: US5346907  
D6: EP-A-564924  
D7: EP-A-441226

**Re Item I**

The amendments filed with the letter dated 16.07.2001 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT:

In amended claim 1, a group of compounds has been defined in which the variable groups R<sup>2</sup>, L<sub>p</sub> and n have values which have been (separately) disclosed in original claims 22, 3 and in the description on pages 19-27. Although claims 22, and 3 are dependent of all previous claims, the group of compounds defined in the amended claim 1 was not disclosed in the original application.

Claims 2-23 are dependent of claim 1 and therefore now refer to subsets of compounds which have not been disclosed in the original application.

In view of the above objections it seemed appropriate to use **the application as originally filed as the basis of this report.**

**Re Item V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Document D1 discloses serine protease inhibitors which have an 1-aminoisoquinoline moiety, which can be substituted (see claim 1 in D1). This teaching is novelty destroying for the subject-matter of claims 1-20,27 and makes the subject-matter of

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/02302

claim 21 obvious. Furthermore it is noted that a disclaimer for these compounds to overcome this novelty objection, will not make the subject-matter of claims 1-20,21,27 inventive.

Document D3 discloses pharmaceutical compounds which have a substituted phenyl moiety, (see claim 1 in D3). This teaching is novelty destroying for claims 1-12,27.

Document D2 discloses serine protease inhibitors which have an 1-aminoisoquinoline moiety (see claim 1 and examples 111ai, 117q and 117r in D2). These compounds are disclaimed in the present application. Such a disclaimer however cannot make the subject-matter of claims 1-12, 25,27 of the present application inventive.

Document D4 discloses pharmaceuticals of formula (I), these compounds and several examples are novelty destroying for claims 1-12,27 of the present application.

Document D5 discloses pharmaceuticals (see claim 1 and examples 61,62), which are novelty destroying for claims 1-12,27 of the present application.

Document D6 discloses pharmaceuticals of formula (I) (see claim 1), which are novelty destroying for claims 1-12,27 of the present application.

Document D7 discloses pharmaceuticals of formula (I) (see claim 1 and example 11), which are novelty destroying for claims 1-12,27 of the present application.

It is a well accepted principle that the pharmaceutical properties of chemical compounds do depend on their chemical structure. The Markush formulas in the claims of the present application are however so extremely broad, that the compounds according to the claims of the present application do not (necessarily) share a specific structural element. Due to this, it is not reasonable to assume that substantially all claimed compounds are serine protease inhibitors. Therefore, the subject-matter of claims 1-24,27 (insofar it is novel) cannot be considered as inventive.